I. Election/Restriction

The Examiner suggests that claims 1, 2, 4-10 and 12-15 have been amended such that they are directed to a non-elected invention. Specifically, the Examiner suggests that the claims have been amended to refer to antisense targeted to two sequences, SEQ ID NO's 10 and 11, which were not included in the scope of the claims as originally presented. Applicants have amended claim 1, and by dependency claims 2, 4-10 and 12-15, to remove the reference to SEQ ID NO: 10 and SEQ ID NO: 11.

II. Rejection of Claims Under 35 U.S.C. 112, Second Paragraph

Claims 1, 2, 4-10 and 12-15 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner suggests that the claims read on a non-elected invention. Applicants have amended the claims as discussed *supra* to remove reference to SEQ ID NO: 10 and SEQ ID NO: 11. Withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 1, 2 and 4-15 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Oguri et al. (1998), in view of Taylor et al. (1999), Baracchini et al. (US Patent No. 5,801,154), and Milner et al. (1997). The Examiner suggests it would have been *prima facie* obvious for one of skill to make antisense targeted to HKR1, including the coding region, translation stop codon, and the 3'-untranslated region, based on the sequence taught by Oguri because methods of making antisense to a known gene is well known in the art as taught by Milner et al., while methods for modifying antisense as claimed are taught by Baracchini et al., and methods of inhibiting expression of HKR1 would be obvious based on what is known in the art. The Examiner further suggests that one of skill would have been motivated to make antisense based on the combination of teaching of Oguri et al. and Taylor et al., since Taylor teaches that antisense can be made and designed with minimal information, while Baracchini et al. provides motivation to make antisense in the claimed size range as well as with the claimed modifications. The Examiner suggests that expectation of success is provided by the teaching of Taylor et al. and Milner et al. Applicants respectfully traverse this rejection.

Oguri et al. (1998) disclose the cloning and identification of HKR1 from a screen of zinc finger transcription factor genes induced in human lung cancer cell lines by exposure to the antitumor platinum drug cisplatin. As acknowledged by the Examiner, nowhere does this patent teach or suggest antisense targeted to specific regions of the human HKR1 of SEQ ID NO: 3. Although the broad regions targeted by the antisense of the instant invention are included in the sequence taught by Oguri et al., these regions are not mentioned in any way in this reference in conjunction with design of antisense.

The secondary references cited by the Examiner fail to overcome the deficiencies in teaching of this primary reference.

Taylor et al. (1999) is a review article on the use of antisense technology. Although this paper indicates that antisense can be designed to inhibit any gene target provided its sequence is known, this paper does not teach or suggest that antisense compounds targeted to specific regions of a gene such as HKR1 of SEQ ID NO: 3 would be active as inhibitors of gene expression. It is only with the teaching of the specification in hand that one of skill would understand that certain regions of the HKR1 gene would be successful targets for antisense compounds.

Milner et al. (1997) teaches a general method for screening antisense molecules. However, nowhere does this paper teach or suggest antisense compounds of any size or type targeted to specific regions of HKR1 nucleic acid molecules as claimed and their use to inhibit gene expression.

Baracchini et al. teaches modifications of antisense oligonucleotides in general. However, nowhere does this reference teach or suggest antisense compounds of any type targeted to specific regions of HKR1 nucleic acid molecules as claimed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as amended, which claim antisense compounds targeted to specific regions of a HKR1 nucleic acid molecule that is listed by sequence, and methods of inhibiting expression of HKR1, and thus cannot render the instant claimed invention obvious. Further, there is no suggestion in the

references cited to combine the teachings of these references as required under MPEP 2143.01. However, in an earnest effort to advance the prosecution of this case, Applicants have amended the claims to refer to targeting specific nucleobase regions of a specific form of HKR1 with antisense. Support for these amendments to the claims can be found throughout the specification as filed but in particular at pages 79-81. Nowhere do the cited references either alone or combined teach targeting of these specific nucleobase regions within SEQ ID NO: 3 with antisense compounds. Further, it is only with the specification in hand that one of skill would understand that these particular regions are successful targets for antisense. Accordingly, withdrawal of this rejection is respectfully requested.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The

attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Respectfully submitted,

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Date: **February 19, 2003**

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 1 has been amended as follows:

1. (thrice amended) A compound 8 to 50 nucleobases in length targeted to nucleobases 70 through 163, nucleobases 397 through 416, nucleobases 506 through 525, nucleobases 594 through 613, nucleobases 644 through 704, nucleobases 732 through 751, nucleobases 760 through 779, nucleobases 907 through 926, nucleobases 1399 through 1418, nucleobases 1726 through 1745 of a coding region, nucleobases 2084 through 2103 of a stop codon region or nucleobases 2108 through 2258, nucleobases 2281 through 2300, nucleobases 2327 through 2388, nucleobases 2468 through 2646, nucleobases 2655 through 2674, or nucleobases 2738 through 2757 of a 3'-untranslated region of a nucleic acid molecule encoding HKR1 of SEQ ID NO: 3, ~~an intron region or an intron:exon junction region of a nucleic acid molecule encoding HKR1 of SEQ ID NO: 10, or an exon region of a nucleic acid molecule encoding HKR1 of SEQ ID NO: 11,~~ wherein said compound specifically hybridizes with one of said regions and inhibits the expression of HKR1.